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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER
CRANE, L

ART UNIT	PAPER NUMBER
1211	13

DATE MAILED:

03/05/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 11/30/95 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire -- 3 -- month(s), ----- days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|-------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice of Draftsman's Patent Drawing Review, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> _____ |

Part II SUMMARY OF ACTION

1. ☒ Claims 40-61 ----- are pending in the application.
Of the above, claims ----- are withdrawn from consideration.
2. ☒ Claims 1-33 and 35-39 ----- have been cancelled.
3. ☐ Claims ----- are allowed.
4. ☒ Claims 40-61 ----- are rejected.
5. ☐ Claims ----- are objected to.
6. ☐ Claims ----- are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on ----- Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on -----, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed -----, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☒ been received ☐ not been received ☐ been filed in parent application, serial no. -----; filed on -----.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

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The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1200, Art Unit 1211.

5 Claims **1-33 and 35-39** have been cancelled.

Newly added claims **40-61** remain in the case and are directed solely to the invention of Group I as originally elected.

The following is a quotation of 35 U.S.C. §103 which forms the basis for all obviousness rejections set forth in this Office action:

10 "A patent may not be obtained though the invention is not identically
disclosed or described as set forth in section 102 of this title, if the
differences between the subject matter sought to be patented and the
prior art are such that the subject matter as a whole would have been
obvious at the time the invention was made to a person having ordinary
15 skill in the art to which said subject matter pertains. Patentability shall
not be negated by the manner in which the invention was made.

20 Subject matter developed by another person, which qualifies as prior
art only under subsection (f) and (g) of section 102 of this title, shall not
preclude patentability under this section where the subject matter and
the claimed invention were, at the time the invention was made, owned
by the same person or subject to an obligation of assignment to the same
person."

Claims **40-59** are rejected under 35 U.S.C. §103 as being unpatentable over Henco et al. '426 in combination with Little '430.

25 The instant claims are directed to a process for DNA purification with the following steps: i) cell lysis and debris removal; ii) contacting with anion exchange resin in buffers of low ionic strength;

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iii) elution of the DNA from the resin by contacting the resin with high ionic strength buffer, iv) following the optional addition of a lower alcohol, or the further optional addition of polyethylene glycol, contacting the eluate with a mineral support material to effect
5 adsorption of the DNA onto the mineral support material, and v) elution of DNA from the support material by contacting the mineral support material with a low ionic strength buffer or with water.

The process disclosed in Henco et al. '426 is in effect a four step process: i) cell lysis/filtration by any one of numerous known methods
10 including the use of detergents, proteolytic enzymes or mechanical procedures (see claim 8) including centrifugation (see column 6, lines 51-56), ii) anion exchange chromatography with a low ionic strength buffer the effect of which is to separate all of the interfering
15 substances/cellular materials from long chain DNA which remains adsorbed on the column optionally in the presence of known DNA precipitants polyethylene glycol or isopropanol (see col. 12, lines 41-42), iii) elution of the long chain DNA from the column adsorbant
20 with high ionic strength buffer, and iv) desalting the DNA by one of several different methods. One method of desalting not mentioned in the Henco disclosure is adsorption chromatography wherein a sample
of DNA is applied to the column adsorbant such as silica gel in the presence of a high ionic strength buffer and separated therefrom by subsequent elution with low ionic strength buffer or water alone.

25 Little '430 at column 7, lines 12-45, discloses one of several examples wherein DNA is extracted from cells of various types using chaotropic ion/enzyme-mediated digestion followed by centrifugation and ultimately chromatographic separation using a commercial diatomaceous earth (Celite) and various buffer solutions. As noted in

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the abstract, Little discloses the application of DNA to the adsorbant from a relative high ionic strength solution and subsequent elution of the adsorbed DNA with a low ionic strength buffer or with water.

5 Applicant's combination of conventional physical separation of cell debris, followed by anionic exchange chromatography and ultimately by mineral support chromatography to effect the purification of DNA is a combination of process steps well known in the prior art and motivated by the disclosures of Henco et al. '426 and Little '430. The failure to teach the specific desalting method of 10 the instant claimed method by Henco '426 has been addressed in the rejection of record by combining with another reference which discloses the utility of classical adsorption chromatography for the purpose of isolating purified DNA in solutions with low net ionic strength. For this reason applicant's claimed process has been found 15 to be nothing more than a combination of Henco with Little et al., wherein Henco provides the motivation to combine by noting the need to desalt the high-ionic-strength solution of DNA produced by anion exchange chromatography (see column 7, lines 44-46; or col. 12, lines 42-43). The specific details of the washing steps, the timing of 20 steps, or the particle characteristics including diameter and pore size are deemed to be variables clearly within the perview of the ordinary practitioner seeking to optimize the Henco process for a specific situation. Therefore, said subject matter is found to include no adequate basis for a finding of patentability in view of the noted 25 prior art.

Therefore, the instant claimed process for DNA purification would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was

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made.

Applicant's arguments filed November 30, 1995 have been fully considered but they are not deemed to be persuasive.

5 Applicant's comments concerning the report of another agency concerning the patentability of the instant claimed subject matter are noted but are not agreed with. The above rejection represents a different combination of prior art necessitated by applicants submission of newly drafted claims.

10 ⁶⁰ Claim ~~35~~ is rejected under 35 U.S.C. §103 as being unpatentable over Hagen et al. '381 in view of Sternberg '142 and Henco et al. '426.

15 The instant claim is directed to a process of nucleic acid purification wherein the first step is a filtration step and the second step contacts the effluent from the first step with an anionic exchange resin.

Hagen et al. '381 at column 8, lines 22-31, discloses the stacking of sheets of filtration materials.

20 Sternberg '142 at column 6, line 9, discloses variation in the porosity of multiple membrane discs usable in the described filtration apparatus and, at line 60, also teaches the application of "ion exchange sheet separation techniques" in concert with the claimed invention.

25 Henco et al. '426 at column 12, lines 23-25 discloses the use of "narrowpore sterile filters ... to retain intact cells or floating cell debris" as part of a DNA separation protocol which subsequently

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used the variation of ionic strength to separate DNA using an anion exchange resin.

Applicant's combination of variable porosity filtration and anionic exchange chromatography to effect the purification of DNA is a combination of process steps well known in the prior art and motivated by the disclosures of Henco et al. '426. The use of a specific filtration methodology (i.e. variation in filter porosity) such as those disclosed by Hagen et al. '381 or Sternberg '142 is deemed to be incorporation of a variation clearly within the perview of the ordinary practitioner seeking to optimize the result of the Henco methodology. Thus, applicants specific process is deemed to have been subject matter clearly within the perview of the ordinary practitioner at the time of the instant filing date. Therefore, said subject matter is found to include no adequate basis for a finding of patentability in view of the noted prior art.

Therefore, the instant claimed method for DNA purification would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

Applicant's arguments with respect to claims now cancelled have been considered but are deemed to be moot in view of the new grounds of rejection.

Claim 61 is rejected under 35 U.S.C. §103 as being unpatentable over Sternberg '142 in view of Henco '426 and Little '430.

The instant claim is directed to a process of nucleic acid purification wherein the first step is a cell lysis/filtration step and

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the second step contacts the effluent from the first step with a mineral support.

The relevant disclosures in Sternberg '142, Henco '426 and Little '430 are described above.

5 Applicant's combination of the steps of variable porosity filtration and "mineral support" chromatography to effect the purification of DNA is a combination of process steps well known in the prior art and motivated by the disclosures of Henco '426 and Little '430. The use of a specific filtration methodology (i.e. variation in filter
10 porosity) such as those disclosed by Sternberg '142 is deemed to be incorporation of a variation clearly within the perview of the ordinary practitioner seeking to optimize the result of the Little method by substitution of a filtration step for a centrifugation step, a change motivated by the disclosure of Henco (see col. 12, Example 2).
15 Thus, applicants specific process is deemed to have been subject matter clearly within the perview of the ordinary practitioner at the time of the instant filing date. Therefore, said subject matter is found to include no adequate basis for a finding of patentability in view of the noted prior art.

20 Therefore, the instant claimed method of DNA purification would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

25 Applicant's arguments with respect to claims now cancelled have been considered but are deemed to be moot in view of the new grounds of rejection.

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Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

5 A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS
FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE
DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS
FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS
10 FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL
AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY
PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE
ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY
EXTENSION FEE PURSUANT TO 37 C.F.R. §1.136(a) WILL BE
15 CALCULATED FROM THE MAILING DATE OF THE ADVISORY
ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR
RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF
THIS FINAL ACTION.

Papers related to this application may be submitted to Group
1200 via facsimile transmission(FAX). The transmission of such
20 papers must conform with the notice published in the Official Gazette
(1096 OG 30, November 15, 1989). The telephone numbers for the
FAX machines operated by Group 1200 are **(703) 308-4556 (for**
Official papers) and **703-308-7923** (for Draft communications).

Any inquiry concerning this communication or earlier
25 communications from the examiner should be directed to Examiner L.
E. Crane whose telephone number is **703-308-4639**. The examiner
can normally be reached between 9:30 AM and 5:00 PM, Monday

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through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kight, can be reached at (703)-308-1235.

- 5 Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1200 receptionist whose telephone number is 703-**308-1235**.

LECrane:lec
3/3/96



JOHN KIGHT
SUPERVISORY PATENT EXAMINER
GROUP 1200